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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/731,366	12/06/2000	Joshua S. Salafsky	0575/60934/JPW/ADM	8346

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Cooper & Dunham LLP
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EXAMINER

COUNTS, GARY W

ART UNIT	PAPER NUMBER
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1641

18

DATE MAILED: 10/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/731,366

Applicant(s)

SALAFSKY ET AL.

Examiner

Gary W. Counts

Art Unit

1641

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on August 8, 2003 (RCE).
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 and 33-38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-28 and 33-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

Status of the claims

The Request for Continued Examination (RCE) filed August 8, 2003 and the amendment filed June 6, 2003 is acknowledged and has been entered.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 21-28 and 33-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21, part (c) "a signal generated" is vague and indefinite. It is unclear what relationship exists between the second harmonic-active label and the signal generated using a surface selective technique.

Claim 28, line 6 "can be" is vague and indefinite. The recitation "can be" is not a positive limitation. It does not constitute a limitation in any patentable sense. Is the amount of the molecule in the medium determined from the change in the signal or not?

Claim 34, part (b) "a signal generated" is vague and indefinite. It is unclear what relationship exists between the second harmonic –active label and the signal generated using a surface selective technique.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1-4, 7, 8, 12, 13, 21, 23, 27, 28, 33, 34, 36 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by anticipated by Quinn et al (EP 0740156).

Quinn et al disclose the use of nonlinear optical methods of surface second-harmonic and sum-frequency generation to detect and quantify antibody-antigen interactions, polynucleotide hybridization and enzyme-substrate complexes (col 1, lines 7-11). Quinn et al disclose that antibodies, antigens, polynucleotides or enzymes are attached to a sensor surface (col 4, lines 1 and 2). Quinn et al disclose that a reporter molecule (label), which possess a molecular excitation close to 2f, may be attached by covalent or other means to the antibody, antigen, or enzyme thereby producing a condition of resonance enhancement (col 2, lines 46-57). Quinn et al disclose that the surface is into contact with a solution, which may contain the complementary species.

Formation of a complex between the complementary species will result in a

Art Unit: 1641

modification of the surface nonlinear optical properties. Measurement of the magnitude, angular dependence or any other parameter dependent on changes of nonlinear optical properties such as surface second-harmonic generation can be used to determine the amount of complex formation at the surface (col 4, lines 39-49).

5. Claims 1-4, 6, 12, 13, 21-23, 34, and 36-38 are rejected under 35 U.S.C. 102(e) as being anticipated by Schultz et al (US 6,180,415).

Schultz et al disclose a method for detecting the presence, information about, a target having a molecular feature of interest (col 5 and 6, col 34, line 6 – col 35 line 33). Schultz et al disclose contacting the target with one or more PRE's (labels) having surface localized molecules to produce an interaction between the molecular feature and the localized molecules. Schultz et al disclose that the target contains a ligand-binding site, and the surface localized molecule is a ligand capable of forming a ligand/ligand-binding complex (col 5, lines 60-67). Schultz et al disclose that the PRE's can accept pulses between 5 to 500 femotsecond for driving second harmonic generation processes. Schultz et al disclose contacting a surface with these PRE's thereby creating an interface at the surface which has target attached thereto wherein the target is not labeled with a non-linear label wherein the target is not detectable at the interface using a surface selective technique and wherein the target is labeled when the PRE comprising the ligand partner for the target attaches to the target and measuring a change in nonlinear optical light at the interface in the presence of the labeled target using a nonlinear optical technique. Schultz et al disclose that the PRE's

Art Unit: 1641

can be used for cell sorting. Schultz et al disclose analyzing a cell type expressing a particular surface antigen using a particular PRE probe (col 49, lines 55-67).

With respect to second harmonic active-label as recited in the instant claims. In the specification on page 2, lines 19-23 the applicant defines that second harmonic active-labels are second harmonic-active moieties which can be attached to a molecule of interest that is not second harmonic active and applicant further defines (page 8, lines 6-11) that a second harmonic refers to a frequency of light that is twice the frequency of a fundamental beam of light and that a second harmonic-active moiety is a substance which when irradiated with a fundamental beam of light generates a second harmonic of the fundamental. Schultz et al disclose that the PRE's (labels) can accept pulses between 5 to 500 femtosecond for driving second harmonic generation. Therefore, Schultz et al disclose second harmonic labels.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 5, 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al (EP 07401156) in view of Mattingly et al (US Patent 5,145,790).

Art Unit: 1641

See above for teachings of Quinn et al.

Quinn et al differ from the instant invention in failing to disclose the molecule being a pollutant.

Mattingly et al disclose specific binding reagents, such as antibodies, for detecting the presence or amount of polychlorinated biphenyls in a test sample (col 2, lines 10-34).

It would have been obvious to one of ordinary skill in the art to use the polychlorinated biphenyl specific antibodies taught by Mattingly et al in the method of Quinn et al because Quinn et al is generic with respect to the analyte that is to be detected and one would use the appropriate reagent, i.e. antibody to detect the desired analyte, in this case polychlorinated biphenyls.

8. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al in view of Buechler et al (US Patent 6,194,222).

See above for teachings of Buechler et al.

Quinn et al differ from the instant invention in failing to disclose the non-specific interaction being an electrostatic interaction.

Buechler et al disclose labels which are bound to the molecule by electrostatic interactions (col 21, lines 1-10). These interactions allow for an immunoassay system that is simple, rapid and reliable. Reliability in an immunoassay system is critical for the accurate measurement of the analyte (col 1, lines 40-43).

It would have been obvious to one of ordinary skill in the art to incorporate electrostatic interactions as taught by Buechler et al for the binding of the second

Art Unit: 1641

harmonic-active moiety to the molecule of Quinn et al because Buechler et al shows that these interactions allow for an immunoassay system that is simple, rapid and reliable.

9. Claim 10, 11 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al in view of Wang et al (US 5,696,157).

See above for teachings of Quinn et al.

Quinn et al differ from the instant invention in failing to disclose that the second harmonic-active label is specific for an amine group.

Wang et al disclose labels, which are specific for amine groups. These amine-reactive dyes are of particular relevance as they are commonly used to label proteins and polypeptides (col 13, lines 50-63). These labels are able to preferentially label a specific ingredient or component in a sample and enable the researcher to determine the presence, quantity or location of that specific ingredient or component (col 1, lines 11-19).

It would have been obvious to one of ordinary skill in the art to substitute the label as taught by Wang et al for the label of Quinn et al because Wang et al shows that these amine labels are of particular relevance as they are commonly used to label proteins and polypeptide and that these labels are able to preferentially label a specific ingredient or component in a sample and enable the researcher to determine the presence, quantity or location of that specific ingredient or component.

Furthermore, since the amine-specific dyes of Wang et al is within the chemical class as disclosed in the specification on page 16, line 24 (amine-

Art Unit: 1641

specific dyes), it is considered that the amine-specific dye of Wang et al would be a second-harmonic active moiety.

With respect to the plurality of individual second harmonic-active labels bound together in a fixed and determinate orientation with respect to each other so as to increase the overall nonlinear susceptibility of the second harmonic-active moiety as recited in the instant claims, the optimum overall nonlinear susceptibility of the second harmonic-active moiety can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art. Further, it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation ." Id. At 458,105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980).

10. Claims 14 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al in view of Eisenthal et al (Photophysics of liquid Interfaces by Second Harmonic Spectroscopy, J.Phys. Chem 1996, 100, vol. 31, 12997-13006).

See above for teachings of Quinn et al.

Art Unit: 1641

Quinn et al differ from the instant invention in failing to disclose an air-water interface and a water-glass interface.

Eisenthal et al disclose the investigation of interface properties using second-harmonic spectroscopy. Eisenthal et al disclose studies of molecules at the silica/water interface and at the air/water interface. The study of molecules at these interfaces provides new information and insights into equilibrium and dynamic processes occurring at interfaces. These liquid interfaces not only are of great scientific interest but also directly impact many areas of medicine and technology (page 12998)

It would have been obvious to one of ordinary skill in the art to incorporate the interfaces as taught by Eisenthal et al into the method of Quinn et al because Eisenthal et al show that the study of molecules at these interfaces provide new information and insights into equilibrium and dynamic processes occurring at interfaces and that these liquid interfaces not only are of great scientific interest but also directly impact many areas of medicine and technology.

11. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al in view of Conboy et al (J. Chem. 1994, 98, 9688-9692).

See above for teachings of Quinn et al.

Quinn et al differ from the instant invention in failing to an oil-water interface.

Conboy et al disclose the investigation of oil-water interfaces. The study of this interface demonstrates the utility of using second harmonic generation to measure properties of the oil-water interface in the absence of any optical

Art Unit: 1641

resonance's and expand the range of systems, which can be examined, by second harmonic generation (abstract and introduction). Conboy et al also disclose that there is a high interest in the characterization of oil-water interfaces because of the central role, which they play in many areas of chemistry, physics, and biology.

It would have been obvious to one of ordinary skill in the art to incorporate the oil-water interface as taught by Conboy et al into the method of Quinn et al because Conboy et al shows that the study of this interface demonstrates the utility of using second harmonic generation to measure properties of oil-water interface in the absence of any optical resonances and expand the range of systems which can be examined by second harmonic generation. Conboy et al also that there is a high interest in the characterization of oil-water interfaces because of the central role, which they play in may areas of chemistry, physics, and biology.

12. Claim s 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al in view of Eisenthal et al US 6,055,051).

See above for teachings of Quinn et al.

Quinn et al differ from the instant invention in failing to disclose the interface is a cell surface.

Eisenthal et al disclose second harmonic generation and sum frequency generation used for surface analysis. Eisenthal et al disclose that the surface to be investigated can be a biological cell where the substance of interest at the surface of the cell (e.g. cell membrane) is detected. Eisenthal et al shows that

Art Unit: 1641

the use of such a surface provide for an analytical tool for ascertaining whether or not the substance will adhere to cells, liposomes, emulsions and similar structures (col 4, line 57- col 5, line 5).

It would have been obvious to one of ordinary skill in the art to incorporate services such as taught by Eisenthal et al into the method of Quinn et al because Eisenthal et al shows that the use of such a surface provide for an analytical tool for ascertaining whether or not the substance will adhere to cells, liposomes, emulsions and similar structures.

13. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al in view of Tadano et al (US 5,962,248).

See above for teachings of Quinn et al.

Quinn et al differ from the instant invention in failing to disclose the molecule being a chloride ion.

Tadano et al disclose a reagent for detecting chloride ions in a sample (col 1, line 66 – col 2, line 10).

It would have been obvious to one of ordinary skill in the art to use the enzyme substrate specific for chloride ions taught by Tadano et al in the method of Quinn et al because Quinn et al is generic with respect to the analyte that is to be detected and one would use the appropriate reagent, i.e. enzyme substrate to detect the desired analyte, in this case chloride ion.

Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude"

Art Unit: 1641

granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1-28 and 33-38 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-17, 19, 24-49, 56- 113, 131 and 132 of copending Application No. 09/907,035. Although the conflicting claims are not identical, they are not patentable distinct from each other because both sets of claims are drawn to methods for detecting molecules at an interface using similar method steps. The instantly recited claims recite a second harmonic-active label while the 09/907,035 claims recite non-linear labels. It is obvious to one skilled in the art that the non-linear labels encompass the second harmonic-active label.

Response to Arguments

16. Applicant's arguments filed June 6, 2003 have been fully considered but they are not persuasive.

Applicant argues that the Quinn et al reference use a reporter molecule to resonantly enhance a signal that is already present and that Quinn et al state that the "second order optical processes originate from the field and structural discontinuity at the interface", and a reporter molecule is used to resonantly

Art Unit: 1641

enhance the surface nonlinear susceptibility. This is not found persuasive because it is the Examiner's position that Quinn et al still read on the new added limitation (i.e. an unlabeled molecule at the interface is undetectable using the surface selective technique) because one skilled in the art would recognize that the second harmonic label would require the second harmonic generation to be detected and if there is no such second harmonic generation label attached to the molecule, such a molecule would not be detected by second harmonic generation. Therefore, it is the Examiner's position that Quinn et al reference still reads on the instantly recited claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (703) 305-1444. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Art Unit: 1641


Gary Counts

Examiner

Art Unit 1641

October 7, 2003



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10/17/03